REMARKS

I. Status of Claims

Claims 1-99 were filed with the original application. Claims 90-99 were canceled and new claim 100 advanced in a preliminary amendment. Claims 19-89 have been canceled pursuant to a restriction requirement, and claims 11-18 were canceled in the previous response. Thus claims 1-18 and 100 are under examination. Claims 1-4, 7, 9 and 10 are rejected under 35 U.S.C. §102, and claims 1-11 and 100 are rejected under 35 U.S.C. §103. The specific grounds for rejection, and applicants' response thereto, are set out in detail below.

II. Rejection Under 35 U.S.C. §102

Claims 1-4, 7, 9 and 10 stand rejected over Dempsey in view Wang and Matthews *et al.* Applicants traverse, but in the interest of advancing the prosecution, claim 1 has been amended to recite the limitations of claim 5, which is not rejected.[1] Therefore, the rejection is believed to be overcome. Reconsideration and withdrawal of the rejection is therefore respectfully requested.

III. Rejection Under 35 U.S.C. §103

Claims 1-11 and 100 stand rejected as obvious over Buchholz *et al.* in view of Bing *et al.* The primary reference is said to teach treating spontaneously hypertensive (SH) rats with staurosporine. However, these rats are not described by the authors as suffering from cardiac hypertrophy. While the *in vivo* methodology section is silent on the age of the animals, two other methods sections indicate that the authors used SH rats aged 15-17 weeks, *i.e.*, less than

[1] It is noted that dependent claim 7 is, in fact, rejected. This is believed to be in error at claim 7 is narrower than non-rejected claim 5.

four months in age. Though Bing *et al.* does indicate that SH rats ***can*** develop cardiac hypertrophy, they do so only during the course of aging (see page 72; right-hand column), with only 59% showing ***pathologic*** heart disease at 19 $\pm$ 2 months. Indeed, persistent hypertension does not even develop until about 2 months of age, followed by "a long period of stable hypertension and ***compensatory*** hypertrophy" (page 72; left-hand column; emphasis added). Thus, Buchholz *et al.* clearly was not ***treating*** hypertrophy, and therefore there is no "inherency" argument for any claim.

Moreover, whatever Bing *et al.* might say about the utility of ***their*** rat model for hypertrophy, ***that apparently is not the model used by Buchholz et al.***, as set forth above. Thus, because Buchholz *et al.* chose to modify they model used by Bing *et al.*, that reference cannot provide any useful teaching on ***treatment of pathologic*** (*i.e.*, not compensatory) ***cardiac hypertrophy or heart failure***, which is what is presently claimed. Buchholz *et al.* does not ever mention cardiac hypertrophy, and both his model and data are ***solely*** directed to the issue of treating spontaneous hypertension. So, given that hypertension can ***lead*** to cardiac hypertrophy, it may be plausible to argue that Buchholz *et al.* suggests ***preventing*** pathologic cardiac hypertrophy or heart failure using staurosporine, but there is no reasonable basis for believing that one could ***treat*** either of those disease states with the same drug. This is because there is no direct link in Buchholz *et al.* between kinase inhibition and cardiac hypertrophy and heart failure. Indeed, though aspects of hypertension may well contribute to development of hypertrophy, there was no reason to believe that hypertension could be treated with staurosporine ***once pathologic cardiac hypertrophy and/or heart failure existed***, much less that one could also treat the pathologic cardiac hypertrophy and/or the ensuing heart failure, as now claimed. In this regard, applicants urge the examiner not to engage in a hindsight analysis where the facial link

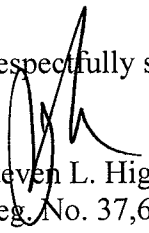
between hypertension and cardiac hypertrophy obscures the fact that the mechanism by which staurosporine (and other PKD inhibitors) successfully treated hypertension could well have ***failed*** in the treatment of pathologic cardiac hypertrophy and/or heart failure.

Therefore, given (a) the lack of any mention or relevant data in Buchholz *et al.* on treating pathologic cardiac hypertrophy or heart failure, (b) the lack of understanding of the underlying molecular mechanisms involved in hypertension and cardiac hypertrophy at the time of filing, and hence (c) the lack of predictability in extrapolating from treating one to treating the other, a *prima facie* case of obviousness will not stand. Reconsideration and withdrawal of the rejection, in view of applicants' comments above, is respectfully requested.

IV. Conclusion

In light of the foregoing, applicants respectfully submit that all claims are in condition for allowance, and an early notification to that effect is earnestly solicited. Should the examiner have any questions regarding this submission, a telephone call to the undersigned is invited.

Respectfully submitted,



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